



NOTES

COMBINED B-CELL & T-CELL DEFICIENCIES

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

- Group of disorders characterized by impaired cellular, humoral immunity
- Diverse genetic causes
- Leads to immunodeficiency, increased susceptibility to recurrent, potentially fatal infections

SIGNS & SYMPTOMS

- Recurrent infections, chronic diarrhea, failure to thrive (FTT), skin rashes

DIAGNOSIS

LAB RESULTS

- Low T lymphocyte, natural killer (NK) cell count
- Normal B lymphocyte count, low immunoglobulins
- Genetic testing to find defect

TREATMENT

OTHER INTERVENTIONS

- Measures to prevent serious infections (e.g. antimicrobial prophylaxis, isolation)

Hematopoietic stem cell transplantation (HSCT)

- If HSCT fails
 - Genetic therapy

ADENOSINE DEAMINASE DEFICIENCY

osms.it/adenosine-deaminase-deficiency

PATHOLOGY & CAUSES

- Absence of ADA → intracellular accumulation of metabolites (e.g. deoxyadenosine), toxic to lymphocytes (esp. T cells)
- Reduction of T, B lymphocytes, NK cell count → combined immunodeficiency
- Autosomal recessive pattern of inheritance

COMPLICATIONS

- Progresses to severe combined immunodeficiency (SCID)

SIGNS & SYMPTOMS

- Presents as SCID early in life
- Neurologic abnormalities (cognitive deficits, behavioral problems, gait abnormalities)

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DIAGNOSIS

LAB RESULTS

- SCID
 - Decreased ADA blood levels

OTHER DIAGNOSTICS

- Genetic testing

TREATMENT

OTHER INTERVENTIONS

- Measures to prevent infections, HSCT
- Gene therapy, enzyme replacement therapy (less effective)

SEVERE COMBINED IMMUNODEFICIENCY (SCID)

osms.it/SCID

PATHOLOGY & CAUSES

- Rare genetic syndrome; disturbance in cell-mediated, humoral immunity
- Combined defects in T, B lymphocyte development, function → severe immunodeficiency

CAUSES

- Underlying causes vary in different forms of SCID
- Cytokine receptor defects, adenosine deaminase (ADA) deficiency (most common)
- Cytokine receptor defects (50–60% of cases)
 - Mutation in gene encoding common γ -chain subunit of interleukin (IL) receptors (IL-2 receptor gamma/IL-2R γ)
- Impaired interleukin signaling required for survival, development, proliferation of lymphocytes (esp. T lymphocytes)
- Profound decrease in lymphocyte count (esp. T, NK-cells)
- B lymphocyte count can be normal, immunoglobulin synthesis defective due to lack of T helper cells

RISK FACTORS

- X-linked recessive pattern of inheritance, more common in individuals who are biologically male

COMPLICATIONS

- Susceptibility to recurrent, severe infections by wide range of microorganisms
 - *Candida albicans*, *Pneumocystis jiroveci*, *Pseudomonas*, cytomegalovirus, varicella
- Without HSCT, death may occur within first year due to fatal infections

SIGNS & SYMPTOMS

- Recurrent infections
- Oral candidiasis presenting with prominent thrush
- Chronic diarrhea → malabsorption, failure to thrive
- Extensive rash
- Morbilliform rash due to reaction of maternal T cells against fetus → graft versus host disease (GVHD)

DIAGNOSIS

DIAGNOSTIC IMAGING

Chest X-ray

- Hypoplasia of lymphoid tissues
 - Absence of thymic shadow; thymic hypoplasia

LAB RESULTS

- Complete blood count (CBC), manual differential
 - Total lymphocyte count, ↓ T cell count, normal B cell count, ↓ immunoglobulin levels
- Polymerase chain reaction (PCR)
 - Measure concentration of T cell receptor excision circles (TRECs); indicative of T cell maturation → decreased levels in SCID

- Genetic testing to find the specific defect
- Lymph node biopsy
 - Hypoplasia of lymphoid tissues where lymphocytes develop
 - Absence of germinal centers

TREATMENT

OTHER INTERVENTIONS

Prevention

- Isolation to prevent serious infections; “bubble baby disease”
- Avoidance of live vaccines
- Antimicrobial prophylaxis
- Immunoglobulin replacement therapy

HSCT

- Curative therapy for most cases
- If HSCT fails
 - Genetic therapy (less effective)